



United States General Accounting Office
Washington, DC 20548

National Security and
International Affairs Division

B-285759

July 20, 2000

The Honorable Mitch McConnell
Chairman
The Honorable Patrick Leahy
Ranking Member
Subcommittee on Foreign Operations
Committee on Appropriations
United States Senate

The Honorable Bill Frist
Chairman
The Honorable Russell Feingold
Ranking Member
Subcommittee on African Affairs
Committee on Foreign Relations
United States Senate

Subject: Global Health: Framework for Infectious Disease Surveillance

In its simplest terms, public health experts define disease surveillance as the generation of "information for action." Infectious disease surveillance provides national and international public health authorities with information that they need to plan and manage efforts to control the diseases.

In recent years, public health officials have expressed concern about the adequacy of the global framework for infectious disease surveillance. In 1995 both the World Health Assembly (the governing body of the World Health Organization) and the U.S. National Science and Technology Council determined that, in light of the global public health threat posed by infectious diseases, existing surveillance arrangements could not be considered adequate.¹ Both organizations, for example, found serious deficiencies in the ability of health systems to diagnose infectious diseases and investigate their sources and modes of transmission. Since then, concern about the

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¹See World Health Assembly Resolution 48.13, "Communicable Disease Prevention and Control: New Emerging and Re-Emerging Infectious Diseases" (Geneva: May 12, 1995); and "Infectious Disease -- A Global Health Threat," Report of the National Science and Technology Council Committee on International Science, Engineering, and Technology Working Group on Emerging and Re-emerging Infectious Diseases (Washington, D.C.: Sept. 1995).

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framework's capacity has increased as public dialogue has intensified on HIV/AIDS, West Nile fever, and other infectious disease threats to U.S. and global public health.

In view of this ongoing concern, you asked us to examine the global infectious disease surveillance framework, with particular emphasis on its operations in developing countries, since infectious diseases are an especially grave problem in these countries. This letter constitutes the first portion of our response to your request. As agreed with your offices, it describes (1) functions involved in infectious disease surveillance and (2) key entities and their roles in the global surveillance and response framework. In the spring of 2001 we intend to provide you with a second report analyzing the framework's strengths and weaknesses and proposals for improving its performance.

RESULTS IN BRIEF

Primary functions in infectious disease surveillance include detecting and reporting cases of disease in target populations, analyzing and confirming this information to identify outbreaks² and clarify longer-term trends, responding to outbreaks when they occur, and supporting longer-term management of disease control programs.

Global surveillance and response efforts are carried out through a loose framework of formal, informal, and ad hoc arrangements linking numerous entities, including elements of national health care systems, as well as the media and internet discussion groups, laboratories and other institutions participating in disease- and region-specific networks, and nongovernmental organizations. National public health authorities bear basic responsibility for surveillance functions. On the global level, the World Health Organization, an agency of the United Nations, plays a central role. The organization works to strengthen national and international surveillance capacity and coordinates international efforts to monitor disease trends and detect and respond to outbreaks. The U.S. Centers for Disease Control and Prevention and the U.S. Department of Defense make significant contributions to these global efforts – for example, through assisting in outbreak response. Foreign assistance agencies, including the multilateral development banks, such as the World Bank, and the U.S. Agency for International Development, as well as private foundations, are important sources of support for strengthening surveillance capacity around the world. This support is generally provided within programs aimed at other objectives, such as control of specific diseases.

BACKGROUND

National security and public health experts agree that infectious diseases pose a substantial direct and indirect threat to U.S. interests. In the most direct sense, experts point out that these diseases pose an increasing danger to the health of the U.S. population. For example, travelers from disease-endemic areas enter the United States every day before sufficient time has passed for them to display symptoms of

²"Outbreak" is used interchangeably with "epidemic" to refer to sudden increases in disease incidence beyond what is considered normal in a given population.

diseases that they may have contracted while abroad. Infectious diseases also pose a substantial obstacle to U.S. efforts to encourage economic growth and betterment in the lives of the poor in the developing world. According to the World Health Organization (WHO), infectious diseases like malaria and tuberculosis account for about half of all premature deaths in the world, and nearly two-thirds of deaths among children under 5 years of age. Infectious diseases are a particular problem in developing countries. Malaria alone, for example, kills more than 1 million people each year, most of them in Africa, and imposes an immense burden in terms of days of productive labor lost to illness. Furthermore, as the National Intelligence Council has observed, there is an indirect but real relationship between high rates of infectious disease and political instability.³

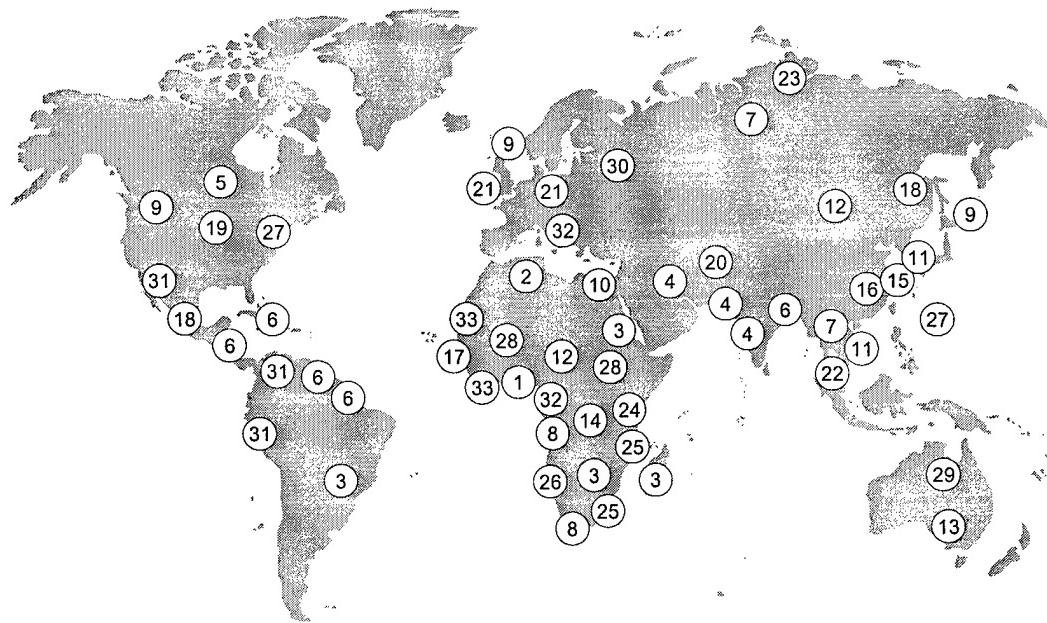
Public health experts at institutions such as WHO and the U.S. Centers for Disease Control and Prevention (CDC) point out that effective action to monitor and control infectious diseases has become more difficult in recent years because of the emergence of new diseases and the reemergence of diseases that were formerly considered to be under control. In the past 3 decades, more than 30 previously unknown diseases have been identified, including Ebola and a number of other deadly hemorrhagic fevers. Yellow fever and tuberculosis, among others, have resumed their former status as major threats to public health. Excessive, uncontrolled use of antimicrobial drugs has complicated the picture further by encouraging the evolution of disease strains that are highly resistant to known forms of treatment.⁴ Figure 1, which shows some of the hundreds of disease outbreaks of international public health importance⁵ identified by WHO since 1994, provides a sense of the challenge now facing international public health authorities.

³For more information on the threats posed by infectious diseases, see "The Global Infectious Disease Threat and Its Implications for the United States," No. NIE 99-17 of the National Intelligence Estimates, National Intelligence Council, (Washington, D.C.: Jan. 2000); and Institute of Medicine, Emerging Infections: Microbial Threats to Health in the United States, (Washington, D.C.: National Academy Press, 1992).

⁴For more information on this topic, see Antimicrobial Resistance: Data to Assess Public Health Threat From Resistant Bacteria Are Limited (GAO/HEHS/NSIAD/RCED-99-132, Apr. 28, 1999).

⁵WHO classifies an outbreak as internationally important when it produces unexpectedly high rates of illness and death, has potential to spread beyond national borders, interferes with international travel or trade, or is likely to require international assistance to control.

Figure 1: Selected Outbreaks of Emerging and Reemerging Infectious Diseases, 1994-99



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|------------------------------------|---|
| 1. Anthrax | 17. Lassa fever |
| 2. Brucellosis | 18. Leptospirosis |
| 3. Cholera | 19. Lyme borreliosis |
| 4. Crimean-Congo hemorrhagic fever | 20. Malaria |
| 5. Cryptosporidiosis | 21. New variant Creutzfeldt-Jakob disease |
| 6. Dengue hemorrhagic fever | 22. Nipah virus |
| 7. Diphtheria | 23. Omsk hemorrhagic fever |
| 8. Ebola hemorrhagic fever | 24. O'nyong-nyong fever |
| 9. E. coli O157 | 25. Plague |
| 10. Echinococcosis | 26. Poliomyelitis |
| 11. Enterovirus 71 | 27. Reston virus |
| 12. Epidemic meningitis | 28. Rift Valley fever |
| 13. Hendra virus | 29. Ross River virus |
| 14. Human monkeypox | 30. Typhoid fever |
| 15. Influenza A (H5N1) | 31. Venezuelan equine encephalitis |
| 16. Influenza A (H9N2) | 32. West Nile fever |
| | 33. Yellow fever |

Note: Enclosure I provides information on these diseases and others mentioned in this letter.

Source: WHO.

INFECTIOUS DISEASE SURVEILLANCE FUNCTIONS

Infectious disease surveillance⁶ is an essential task for public health authorities in every country. This task involves four primary functions. The first of these is detecting cases of disease in the population and reporting this information so that it can be used in public health decision-making. The second is analyzing and confirming reported information to detect outbreaks and identify longer-term disease trends. The third function is providing timely and appropriate responses to disease outbreaks. Finally, surveillance involves providing information to assist in longer-term management of health care policies and programs. Each of these functions is an integral part of disease surveillance.

Detecting and Reporting Disease

The most basic surveillance functions are detecting disease in the population being surveyed and reporting relevant data so that the data may inform public health decision-making. A variety of approaches to performing these functions are available, including passive and active surveillance, and “sentinel” and “syndromic” reporting. These approaches are not mutually exclusive – they can be, and often are, combined to provide a fuller understanding of the incidence of infectious disease in a target population.

“Passive” surveillance is the most broadly employed approach. In this approach, national or district-level authorities prepare a list of “notifiable” diseases, guidelines for diagnosing these diseases, and specifications for information to be gathered when these diseases are detected (for example, the patient’s age and the date of onset of disease.) National or district level authorities then rely upon local health care providers to detect cases of disease and report information on these cases as specified.⁷ When instituting passive reporting requirements, national or district authorities must make arrangements for collecting this information from localities throughout the country or region. Public health experts at WHO commented that responsible authorities should also create feedback mechanisms to let health care providers know that the information they are providing is being put to use. Feedback, in the form of regular bulletins on epidemiological trends, progress toward disease control targets, or efforts to control outbreaks, can help motivate health care providers to continue investing the effort required to meet reporting requirements.

Deciding which diseases should be “notifiable” is a key element in this process. WHO’s International Health Regulations require member countries to monitor only

⁶Public health surveillance can also cover other concerns, like noninfectious diseases and accidental injuries. This report focuses only on infectious diseases.

⁷Other sources, including laboratories and community leaders, may also be enlisted in the interest of fuller reporting.

three diseases: cholera, plague, and yellow fever.⁸ Beyond this, each country must decide upon a list of diseases that will be subject to regular reporting. In the United States, more than 50 diseases are considered "notifiable" at the national level.⁹ Developing country lists are usually less extensive. For example, the Ethiopian Ministry of Health had 17 diseases under surveillance as of 1999. Developing countries commonly emphasize diseases that the donor community has targeted for control or outright eradication, including polio and other vaccine-preventable diseases.¹⁰

"Active" surveillance is often employed to help compensate for the reporting shortfalls commonly encountered in passive reporting arrangements. In this approach, health workers from the district or national levels "make the rounds" to seek out possible cases. Such efforts are commonly made to ensure complete reporting in situations where an epidemic is occurring or is deemed likely to occur or during campaigns to eradicate individual diseases. For example, active surveillance has been a prominent feature of the international campaign to eradicate polio. These efforts may be organized into regular surveys.

"Sentinel" reporting is also employed to supplement the information obtained through broadly focused passive reporting. Sentinel reporting relies on comparatively small numbers of specially equipped practitioners to provide information on diseases of particular concern. One common example is the enlistment of sexually transmitted disease clinics to monitor HIV incidence through blood testing. Sentinel reporting is particularly useful for generating "early warnings" of changes in disease patterns, including the emergence of new diseases.

"Syndromic" reporting is another tool that can be employed to increase a system's effective reach – at a cost of reduced specificity in the information reported. In this approach, health care providers are asked to report syndromes – that is, collections of symptoms – rather than attempting to make exact diagnoses that are beyond their capacity. This can be particularly useful in developing country settings where health care providers may have very limited ability to make firm diagnoses themselves or to refer questionable cases to laboratories for rapid clarification.

⁸In addition to requiring countries to report cases of these three diseases to the World Health Organization, the regulations set out rules for countries to follow in instituting measures to prevent the spread of these diseases at points of embarkation, during international travel, and at points of entry. The regulations have been in force since 1971. WHO is currently engaged in an effort to expand and strengthen the regulations.

⁹In the U.S. federal system, the individual states have principal responsibility for public health functions, including surveillance. National reporting is voluntary – each state decides which diseases will be reported to its health department and which information it will pass on to CDC. For more information on surveillance in the United States, see Emerging Infectious Diseases: Consensus Needed on Laboratory Capacity Could Strengthen Surveillance (GAO/HEHS-99-26, Feb. 5, 1999).

¹⁰WHO's efforts to control "vaccine-preventable" diseases have historically targeted diphtheria, measles, polio, pertussis, tetanus, and tuberculosis.

Analyzing and Confirming Disease Information

Public health officials at the district, national, and (in some cases) international levels are responsible for aggregating and analyzing information reported from lower levels. These activities often extend to providing laboratory analysis and other investigative assistance to confirm or clarify initial diagnoses made by individual health care providers – especially in developing countries where local diagnostic capacity is often quite limited. Higher-level data aggregation is particularly important where cases are too dispersed in time or location to be recognized at the local level.

In carrying out these analyses and investigations, responsible officials examine disease information along three basic dimensions: person, time, and location. In other words, they seek to clarify who is getting sick, when they are getting sick, and where. Epidemiologists use this information to calculate rates of sickness and death in specific populations and at specific times, and to compare these rates over time and location. In combination with identifying the pathogens causing particular illnesses, the answers to these questions provide a basis for taking action. For example, by analyzing who was getting sick and when, public health officials in the former Soviet Union were able to determine that a 1990-95 resurgence of diphtheria had been caused by gaps in the diphtheria immunization program.

Public health officials responsible for analyzing and interpreting disease data must proceed with caution. Among other things, these officials must take into account the proportion of disease cases health care providers are likely to detect and report. This is affected by such factors as the likelihood that persons with certain health conditions will seek medical care. People with sexually transmitted diseases, for example, may be reluctant to seek treatment. To complicate matters, these proportions are subject to change. For example, increased public concern about a particular disease may increase the likelihood that people who believe they have this disease seek treatment -- and that health care providers report seeing these patients. One of the first steps that an official faced with an apparent increase in reporting of a particular disease must take is to determine whether this increase might be due to such changes.¹¹

Responsible officials must also take into account the likelihood of health care providers being able to make accurate diagnoses. Even in advanced countries like the United States, attaining a high degree of certainty in patient diagnoses can be a challenge. Health care providers may be unfamiliar with some diseases, or they may lack the ability to distinguish among diseases with similar symptoms. Health care providers rarely have immediate access to comprehensive laboratory facilities, and, in developing countries in particular, may lack training in making diagnoses and access to even the simplest diagnostic tests.

¹¹U.S. Agency for International Development officials observed that strengthening a surveillance system may result in an apparent surge in the disease or diseases being monitored. The officials pointed out that unless policymakers anticipate such surges, they may initially be disappointed when surveillance investments do not appear to lead to a drop in disease rates.

WHO guidelines for clinical (that is, symptom-based) diagnosis of dengue fever provide a sense of the difficulty of making confident diagnoses. WHO defines a clinical case of dengue fever as an acute illness of 2-7 days' duration characterized by fever and two or more of a number of other symptoms. Several of these, like headache, rash, and muscle or joint pain, may be caused by a number of other disease agents, in addition to the dengue virus. WHO officials noted that national or district public health officials can increase the reliability of diagnostic reports from the field by ensuring that health care providers throughout the country or region employ clear, consistent case definitions.

Responding to Epidemics

In addition to detecting unusual patterns of disease and investigating their causes, responsible public health officials must determine the likely seriousness of an epidemic in medical and socioeconomic terms and, in cooperation with others, devise and carry out appropriate response measures.

The likely course of events in any given epidemic will vary depending upon the pathogen involved and local circumstances – including weather, prevailing living conditions, and the effective reach of existing public health facilities. Public health officials who have an understanding of the likely course of events in a given situation will be in a better position to develop an appropriate response. Ebola hemorrhagic fever and meningococcal meningitis – two diseases of particular concern in Africa – provide an instructive comparison.

According to WHO officials, most Ebola transmission takes place through direct physical contact with the skin or mucous membranes of persons currently sick with this disease. Consequently, Ebola outbreaks actually endanger relatively small numbers of people and can be halted relatively easily through application of containment measures in the affected locality. Meningococcal meningitis, in contrast, is most often acquired through inhaling respiratory droplets from infected but asymptomatic carriers of the disease. The disease presents a high risk of widespread transmission, especially in dry weather when people's mucous membranes become irritated. Africa's meningitis belt countries experience periodic epidemics that cross national boundaries to infect large numbers of people.¹² Proper responses to these epidemics include mass vaccination of threatened populations and the delivery of appropriate medicine to large numbers of sick people.¹³

Epidemic response measures include interventions designed to ensure that persons already sick with a disease receive proper care and to reduce or eliminate further transmission. One element in such a response may be procurement and distribution of diagnostic materials (and associated training) that will permit health care

¹²The African meningitis belt, which stretches from Senegal to Ethiopia, has historically experienced epidemic waves at 8- to 12-year intervals. The last such wave – in 1996 – resulted in more than 250,000 cases and 25,000 deaths in Burkina Faso, Niger, Nigeria, and other countries.

¹³One element in the Ghanaian response to a 1997 epidemic, for example, was distribution of nearly 1.9 million doses of vaccine.

providers to identify disease pathogens faster and with more certainty. Both health care providers and members of the public (who may need to care for sick family members) may require instruction on appropriate case management techniques – that is, how to care for persons infected with the disease in question. In major epidemics, it may become necessary for public health officials to simplify normal approaches to case management in order to permit the health system to cope with unusually large numbers of patients.¹⁴ Health systems may need to rapidly expand available treatment facilities and provide them with supplies of antimicrobial drugs, vaccines (if appropriate), and other materials that may be needed to combat the epidemic. Logistics – that is, managing the procurement, delivery, and distribution of these supplies – can be a major challenge.

Effective communication with concerned members of the public is an important element in epidemic response. An epidemic's direct consequences (that is, sickness and death among those who contract a disease) may be substantially amplified by adverse public reaction. Unconfirmed, misinformed, or incomplete announcements can confuse health care providers and members of the public alike and prompt them to take inappropriate actions. In cooperation with the media and with the support of national leaders, public health officials must work from the earliest moment to provide the public with accurate information on the disease's transmissibility and means of treatment.

Effective epidemic response can require the participation of many elements of society, including (in addition to health care providers) political leaders at varying levels of authority, nongovernmental organizations, and – in some situations – representatives from the agricultural, veterinary, environmental, public works, law enforcement, and transportation sectors. WHO officials therefore strongly recommend creation of epidemic response committees to coordinate action by all parties. This is particularly important in developing countries where, because of local institutional weaknesses and lack of resources, outside agencies such as WHO and CDC are likely to play a vital role in epidemic response.

Reassessing Longer-term Policies and Programs

Surveillance systems are important sources of information for longer-term management of health programs at all levels. Over the long term, surveillance system can provide public health authorities with insight into changing disease patterns. For example, surveillance systems are providing international public health authorities with information on the worldwide spread of HIV/AIDS and strains of tuberculosis that are resistant to antimicrobial drugs. Information on such trends can be used to inform decision-making on health care priorities and associated resource allocation decisions.

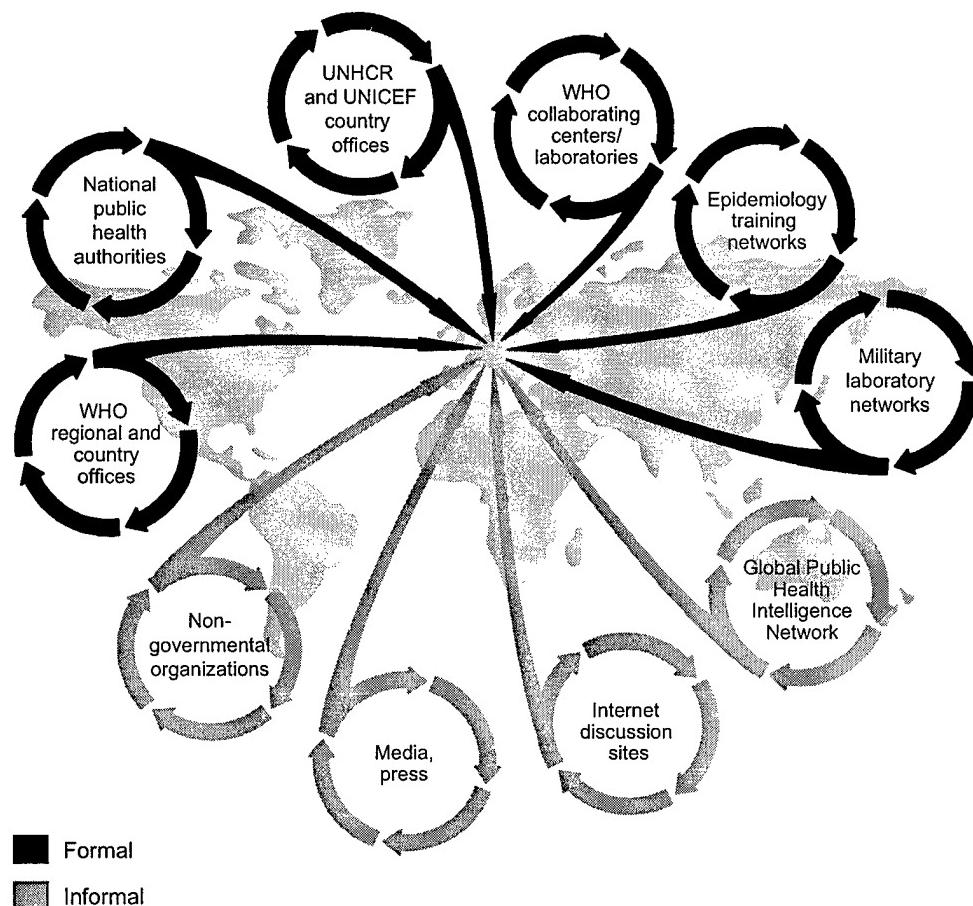
¹⁴During meningococcal meningitis epidemics, for example, WHO guidance indicates that responsible officials may wish to consider adopting a single dose of oily chloramphenicol as the standard antibiotic intervention, rather than other options, which involve administration of drugs over several days.

Surveillance systems are also important tools in monitoring, assessing, and refining disease control interventions. At the international level, the most well-known example is the use of surveillance to manage the ongoing effort to eradicate polio. Surveillance data are also important inputs to decision-making at the national and local levels. For example, continued surveillance was important in assessing the impact of revised vaccination practices adopted in the wake of the diphtheria epidemic in the former Soviet Union which was mentioned earlier in this letter. Officials at the U.S. Agency for International Development (USAID) and WHO observed, however, that developing countries' surveillance efforts often do not produce information that can be relied upon to document changes in the health impact of major diseases or the impact of disease control programs.

GLOBAL SURVEILLANCE: A NETWORK OF NETWORKS

As acknowledged in the previous discussion of surveillance functions, basic responsibility for monitoring and responding to disease trends lies with national governments around the world. On the global level, however, disease monitoring and response functions are carried out through a framework of formal, informal, and ad hoc arrangements that WHO officials characterize as a "network of networks." In addition to public health officials in ministries of health and national disease control centers in individual countries, key entities in this framework include (1) WHO, (2) the media and internet discussion groups, (3) disease and region-specific networks (which include infectious disease laboratories), (4) nongovernmental organizations, and (5) foreign assistance agencies and private foundations. However, since support for surveillance activities is generally provided within programs aimed at other objectives (like control of specific diseases), these organizations could not readily estimate their overall expenditures for surveillance activities. Figure 2 presents one illustration of this global framework. A brief overview of the key entities follows.

Figure 2: Global Surveillance of Communicable Diseases: A Network of Networks



Source: WHO.

The World Health Organization

WHO plays a central role in the global disease surveillance and response framework. However, WHO officials are quick to point out that the organization cannot perform these functions alone – they place great emphasis on their role in marshaling and coordinating relevant efforts by multiple parties, including technical and donor agencies around the world.

WHO itself can be regarded as a network of organizations, as it is organized along both geographic and functional lines. WHO maintains six regional offices.¹⁵ Each of these maintains a network of country representative offices and formulates policies

¹⁵WHO maintains regional offices for Africa, the Americas, the eastern Mediterranean, Europe, Southeast Asia, and the western Pacific. The regional office for the Americas, also known as the "Pan-American Health Organization," predates WHO.

and undertakes initiatives within its own area of the world in line with WHO's global priorities. With regard to surveillance, for example, WHO's Western Pacific Regional Office is working to strengthen influenza surveillance and epidemic response planning in its region, while WHO's regional office for the Americas is encouraging integration of disease surveillance activities among countries that share the Amazon River basin, as well as in other regions of Latin America.

Within WHO's Geneva headquarters, the Division of Communicable Diseases plays a central role. The Division's mission is to "strengthen national and international capacity in the surveillance, prevention and control of infectious diseases." However, other headquarters units also make contributions. For example, the Department for Vaccines and Biologicals coordinates worldwide efforts to control vaccine-preventable diseases. Strengthening national and global surveillance for these diseases is an important element in this office's work.¹⁶ Similarly, WHO maintains a separate department for HIV/AIDS and other sexually transmitted infections, and surveillance is a key element in this office's mission as well.

To strengthen surveillance and control at the national level, WHO generates and disseminates standards and guidelines for creating, operating, and assessing national disease surveillance systems and supports and disseminates the results of research into surveillance and control issues. WHO works with national governments to assess and redesign national surveillance strategies and to improve surveillance capacity through, for example, training in epidemiologic and laboratory techniques and emphasizing improved communications. At the regional and global levels, WHO collaborates with numerous other organizations to create, maintain, and improve networks of laboratories and other institutions and administers the International Health Regulations.

In 1997, WHO created an "outbreak verification" mechanism in order to generate timely, accurate information on disease outbreaks around the world and to provide the organization with a basis for encouraging a rapid and coordinated response.¹⁷ The system draws from multiple sources -- including the Global Public Health Intelligence Network, a worldwide web search engine developed and maintained by Health Canada. When suspected outbreaks of international importance are identified, WHO staff seek confirmation from health authorities in the countries involved and others who may have knowledge of the events in question. Outside laboratories like those maintained by CDC are often asked to perform analyses to identify the pathogens that are causing the outbreak. Having clarified the situation, WHO disseminates accurate

¹⁶For more information on this department's activities, see Global Health: Factors Contributing to Low Vaccination Rates in Developing Countries (GAO/NSIAD-00-4, Oct. 15, 1999) and Global Health: Summary of Conference on Immunization in Developing Countries (GAO/NSIAD-00-95, Mar. 1, 2000).

¹⁷WHO is currently working with multiple international partners, including prominent nongovernmental organizations and member government agencies, to improve the global community's outbreak response capacity through creation of a formal "Global Outbreak Alert and Response Network."

information on the outbreak and works to organize a response.¹⁸ Response efforts can involve numerous partners. For example, the response to one epidemic of unexplained origin in Kenya and Somalia, later determined to be Rift Valley fever, involved representatives from 31 different governmental and nongovernmental agencies, including elements of CDC and the Department of Defense. Enclosure II provides more detail on this outbreak.

The Media and Internet Discussion Groups

Nongovernment sources – including the media and Internet discussion groups – are playing an increasingly important role in infectious disease surveillance and response. For example, WHO has found that 71 percent of the outbreaks confirmed through its outbreak verification procedure in a recent 2-year period were initially reported through informal or unofficial sources, including the media and Internet discussion groups, as well as nongovernmental organizations.

As agents of a government-sponsored body, WHO officials must normally obtain country consent before disseminating information on outbreaks. WHO officials note that their efforts to verify – and notify – infectious disease outbreaks in a timely manner have sometimes been delayed by national governments concerned about the potential adverse consequences of acknowledging that outbreaks are taking place in their countries. However, the expansion of media coverage and, especially, electronic communication via the Internet, is decreasing the likelihood that national officials can successfully keep outbreaks hidden for any length of time.

As in so many other areas, Internet discussion groups have become an important means of sharing timely information on infectious disease events and trends around the world. A number of disease-specific and regionally focused surveillance networks (described at greater length later) maintain such discussion groups. For example, organizations and individuals interested in eradication of dracunculiasis (guinea worm disease) share information through a WHO-maintained Internet discussion group known as "Dracerad." Other groups are more generally focused. One of these – ProMED – is particularly important. A program of the International Society for Infectious Diseases, ProMED was created in 1994 to establish a direct relationship among scientists and doctors around the world by making it possible for all to share information and discuss emerging disease concerns on a timely basis. More than 18,000 people subscribe to the ProMED listserve, which provides information on human, animal, and plant diseases. The system generates approximately seven postings per day, 7 days a week. While ProMED accepts information from any source, expert moderators screen this information before it is posted.

While making a contribution to timely outbreak identification, the media can also contribute to effective outbreak response. According to WHO, for example, the local affiliate of the British Broadcasting Corporation made a valuable contribution to the

¹⁸WHO posts information on confirmed outbreaks at http://www.who.int/emc/outbreak_news/index.html.

international response to the previously mentioned Rift Valley fever outbreak in East Africa. The affiliate's broadcasts both drew attention to the problem among national and international authorities and helped provided the public with accurate information about the epidemic. According to USAID, the Voice of America has increased its reporting on health issues of interest in developing countries, including infectious diseases of particular concern, like HIV/AIDS, and outbreaks in these countries.

Disease-specific Networks

To encourage the advancement and efficient application of expertise on specific diseases (or categories of disease), WHO has fostered the creation of international networks focusing on specific types of disease. Infectious disease laboratories form the core of these networks. As already indicated, laboratory support is a critical element in infectious disease surveillance, but capacity to provide this support is unevenly distributed around the world and is particularly lacking in developing countries. Networking helps make these laboratory facilities accessible to the global community.

Examples of formal global networks include those focusing on influenza, polio, and antimicrobial resistance. These networks perform a variety of functions. For example, laboratories in 83 countries participate in WHO's global Influenza Program, which monitors the evolution and global distribution of influenza virus and applies this information to make annual recommendations concerning the composition of influenza vaccines. One hundred and forty-eight laboratories around the world participate in the Global Network for Polio Eradication. Participating laboratories cooperate to confirm suspected cases of polio and to distinguish among strains of the disease. These analyses provide the basis for appropriately targeted response measures when polio cases are confirmed and help participating scientists to advance global understanding of the evolution of the polio virus – laying the groundwork for more effective response measures in coming years. In collaboration with the French National Institute for Health and Medical Research and the United Kingdom's Department for International Development, WHO recently inaugurated an "Anti-Microbial Resistance Information Bank" – an internet service that is intended to encourage greater collaboration among antimicrobial resistance monitoring efforts throughout the world.

Public health professionals with whom we spoke noted that, in practice, informal networking among laboratories is often the key to addressing pressing problems. For example, in the fall of 1998, Malaysia experienced a sharp increase in cases of illness and death from a disease that was initially identified as Japanese encephalitis. However, in March 1999, scientists at the University of Malaysia determined that a different viral agent was likely causing the outbreak. Finding themselves unable to precisely identify this agent, the Malaysian scientists contacted CDC for assistance. Malaysian personnel subsequently traveled to CDC's Division of Vector-Borne Infectious Diseases in Fort Collins, Colorado with samples for analysis. Laboratory work at the Colorado facility advanced the investigation, which concluded when staff from the CDC's National Center for Infectious Diseases in Atlanta, Georgia, identified

the previously unknown pathogen, named the "Nipah" virus, that had caused the outbreak.¹⁹

Many of the institutions that participate in these networks have been designated as official WHO "collaborating centers." WHO collaborating centers provide training, research, consulting, and other forms of service to assist the organization in pursuing its objectives. Approximately 1,300 institutions carry this designation, though WHO officials observed that these institutions vary considerably in their ability to contribute to international operations. WHO's Department of Communicable Disease Surveillance and Response maintains active relationships with approximately 270 of the centers. Figure 3 displays one set of WHO collaborating centers.

Figure 3: WHO Collaborating Centers for Arboviruses and Hemorrhagic Fevers



Note: An arbovirus is one that is transmitted by mosquitoes or other arthropods. These include the pathogens that cause yellow fever and dengue. Enclosure III contains a list of the collaborating centers shown on this map.

Source: WHO.

¹⁹The virus was named after the town where the original sample for analysis was obtained. Officials from CDC noted that after identifying this virus they continued to work with their Malaysian counterparts to control the epidemic and institute measures to halt further transmission.

Contributions From the Centers for Disease Control and Prevention

With 30 WHO-designated collaborating centers focused on particular infectious diseases and with five research centers abroad,²⁰ CDC constitutes the single largest pool of expertise and resources available to the international system. As of the spring of 2000, nearly 90 staff members were working abroad on infectious-disease related matters. CDC devoted approximately \$100 million in fiscal year 1999 to international activities related to infectious disease surveillance, control, and prevention, including laboratory analysis to identify pathogens involved in outbreaks of international significance. CDC could not provide a separate accounting for surveillance activities alone. CDC has been an active participant in WHO efforts to provide epidemiology training to developing countries. For example, it has helped to establish national field epidemiology training programs in over 20 countries.²¹

Military Networks

Particularly in developing countries, military health care systems may have capacities that match or exceed those available in the civilian sector. Countries with substantial worldwide commitments have an especially strong incentive to develop the capacity of their military health care systems in order to protect their own personnel around the world. WHO is working to encourage cooperation in surveillance activities among laboratories worldwide that are operated by national military establishments.

Contributions From the U.S. Department of Defense

The U.S. Department of Defense plays a noteworthy role in global surveillance and response through its Global Emerging Infections Surveillance and Response System. This system links the Department's overseas laboratories and its service-specific preventative medicine programs in a coordinated program focused on contributing to timely recognition and control of emerging and reemerging infections. The Department maintains medical research laboratories in five foreign countries (Egypt, Kenya, Indonesia, Peru, and Thailand). According to Defense officials, these laboratories assist in conducting surveillance for influenza, drug-resistant malaria, intestinal organisms, and hemorrhagic fevers and help to build local capacity around the world. The Department's research facilities in Indonesia and Egypt and three facilities in the United States have been designated as WHO Collaborating Centers for infectious disease.²² The Department budgeted approximately \$7 million to support Global Emerging Infections Surveillance and Response System activities during fiscal year 2000.

²⁰CDC maintains research facilities in Botswana, Côte d'Ivoire, Guatemala, Kenya, and Thailand.

²¹Officials from CDC noted that with support from CDC and WHO, these national programs have themselves become significant contributors to global surveillance and have created their own network for sharing information and expertise.

²²These are the U.S. Army Medical Research Institute of Infectious Disease, the Armed Forces Institute of Pathology's Department of Infectious and Parasitic Diseases Pathology, and the Division of Experimental Therapeutics at the Walter Reed Army Institute of Research.

Region-specific Networks

With WHO's encouragement, public health authorities in a number of regions have fostered the creation of regional surveillance networks. In 1996, for example, the secretariat of the Pacific Community launched the Pacific Public Health Surveillance Network to improve surveillance and response in the Community's 22 member states and territories.²³ One prominent feature of this network is the sharing of surveillance data through the Internet. This is also a prominent feature of some other subregional networks, such as the European Union's Eurosurveillance project and the Mekong Basin Disease Surveillance System. Twenty-one Caribbean countries benefit from the activities of the Caribbean Epidemiology Center. This center – a decentralized unit of WHO's regional office for the Americas -- provides a range of epidemiological and laboratory analysis services to participating countries.

While Internet capacity is extremely limited in Africa, this continent is nonetheless the location of some of the more ambitious efforts to encourage subregional cooperation for more effective surveillance and response. In the wake of the major meningitis epidemics in 1995 and 1996, WHO fostered the creation of an International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control in the African meningitis belt countries. This group, which includes concerned national governments, nongovernmental organizations, and makers of vaccines and other medical supplies, works to improve meningitis surveillance and foster greater preparedness for epidemic response in this region. WHO's Africa region is also encouraging greater collaboration for surveillance within five subregional "epidemiological blocks" that face similar sets of disease challenges. According to WHO officials, this effort involves creation and implementation of national plans to strengthen surveillance as well as the establishment of subregional laboratory networks, and the promotion of improved communications among public health officials within these "blocks." This effort emphasizes the integration of existing, disease-specific surveillance operations.

Nongovernmental Organizations

Nongovernmental organizations play a vital role in disease surveillance and control in many developing countries. Even when "normal" conditions prevail, many people in the world's poorest countries do not receive health services from government-supported clinics or private practitioners but from organizations such as Doctors Without Borders and Catholic Relief Services. Because they constitute the professional presence in the field, these organizations conduct surveillance and participate in outbreak response efforts when necessary.

These organizations play a particularly vital role in the increasing portion of the world that is plagued by complex humanitarian emergencies -- humanitarian crises in

²³The members of the Community are the Cook Islands, the Federated States of Micronesia, Fiji, Guam, Kiribati, the Northern Marianas, the Marshall Islands, Nauru, Niue, New Caledonia, Palau, Papua-New Guinea, Pitcairn Island, French Polynesia, the Solomon Islands, Samoa, American Samoa, Tokelau, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna.

countries or regions where there has been total or considerable breakdown of authority resulting from internal or external conflict and where a situation has developed that requires action going beyond the mandate or capacity of any single agency. These emergencies may last for many years. According to WHO, about half of all disease outbreaks of international importance are now occurring in such situations.²⁴ With some noteworthy exceptions (Kosovo, Afghanistan, and East Timor) most of the more than 100 million people currently affected by such emergencies live in Africa. According to WHO, populations in 11 African countries are affected by complex emergencies.²⁵ Figure 4 illustrates the living conditions generated by such an emergency in the eastern portion of the Democratic Republic of Congo in 1997.

Figure 4: Complex Emergency Conditions: Refugees in Eastern Democratic Republic of Congo



Source: S. Collins, through WHO.

²⁴WHO found that 49 percent of the outbreaks identified through its Outbreak Verification process during July 1997 through July 1999 took place in complex emergency situations. This calculation excludes outbreaks taking place among refugees living in stable circumstances.

²⁵The 11 countries are Angola, Burundi, Congo/Brazzaville, Democratic Republic of Congo, Liberia, Rwanda, Sierra Leone, Somalia, Sudan, Tanzania, and Uganda.

Responsibility for arranging a humanitarian response to complex emergencies falls to the U.N.'s Office for the Coordination of Humanitarian Affairs, and, according to WHO, this organization usually relies upon either WHO or the United Nations Children's Fund to coordinate the health sector portion of these responses. However, responsibility for actually delivering health services – and hence front-line responsibility for disease surveillance – most often falls to health-oriented nongovernmental organizations. In southern Sudan, for example, where government services ceased functioning years ago, nongovernmental organizations, including Doctors Without Borders and Oxfam, provide such health care services as are available.

Given the difficulty of detecting and addressing disease in these populations, such outbreaks may generate high levels of death and disease before they are addressed. For example, a cholera outbreak in eastern Democratic Republic of Congo in 1994 killed 12,000 people in 3 weeks. In the same region several years later, a measles outbreak spread to over 1,000 children before being detected.

Foreign Assistance Agencies and Private Foundations

Foreign assistance agencies like the USAID and the multilateral development banks, as well as private foundations, are important sources of support for strengthening surveillance activities – both within individual developing countries and at regional and global levels. However, because these organizations most often support surveillance activities as elements within (a) programs aimed at controlling or eradicating specific diseases or (b) broadly focused health sector improvement or infectious disease control programs, it is difficult to estimate the amount of funds that they provide for surveillance as such with any precision.

For example, over the last 30 years many organizations, including the World Bank, the African Development Bank, USAID, and private companies and foundations, have supported an intensive effort to eradicate river blindness – a disease that was once endemic in much of Africa. A portion of the more than \$500 million devoted to this cause to date has gone toward surveillance, but an estimate of the portion devoted to this purpose is not available. Surveillance activities have also received substantial support through donor assistance to international initiatives aimed at (among other things) eradicating guinea worm disease, addressing the global HIV/AIDS and tuberculosis pandemics, and controlling vaccine-preventable diseases. The international campaign to eradicate polio, in particular, has focused donor resources on establishing functional polio case detection and response mechanisms in every country, no matter how limited these countries' general surveillance capacity.

We identified a few major foreign assistance agency efforts to improve national infectious disease control programs, with substantial emphasis on upgrading surveillance. For example, the World Bank is providing a total of approximately \$150 million to strengthen the national infectious disease surveillance and control systems in Argentina and Brazil. The Asian Development Bank is providing \$87 million to support a similar effort in Indonesia. Many other agency-supported projects contain surveillance components. For example, the African Development Bank identified

surveillance components in 15 current projects aimed at a variety of purposes, including creating national health management systems and strengthening disease-specific control or eradication programs. USAID identified about \$11 million in support for surveillance-specific operations within a variety of country-specific and regional health sector programs during fiscal year 1999. However, agency officials noted that this figure does not present a complete picture of USAID investments in surveillance. It does not include surveillance support provided through other programs, including those focused on child survival and on specific diseases such as polio, tuberculosis, and HIV/AIDS, where meaningful separation of surveillance funding from funds devoted to other purposes is quite difficult.

From 1998 through 1999, "extrabudgetary" funds – that is, contributions from foreign assistance agencies and private foundations – provided more than 70 percent of the \$28.2 million budget of WHO's Department of Communicable Disease Surveillance and Response.²⁶ Donor contributions and temporary assignment of personnel from technical agencies such as CDC have enabled this office to more than double its staffing level. Financial support from foreign assistance agencies and private foundations has also made possible initiatives like that currently being undertaken to strengthen surveillance and response capacity within subregional epidemiological blocks in Africa. The WHO Africa regional office's project to introduce integrated disease surveillance in the West African epidemiological block, for example, is being supported by (among others) USAID, the European Union, the United Kingdom's Department for International Development, and the Rockefeller and United Nations Foundations.

AGENCY COMMENTS

We received oral comments on a draft of this report from the Departments of State, Defense, and Health and Human Services (including CDC); USAID; the offices of the U.S. Executive Directors of the World Bank, the Asian Development Bank, and the African Development Bank; and the World Health Organization. These institutions stated that the report provided an accurate overview of surveillance functions and correctly identified and described the roles played by major participants in global infectious disease surveillance. Some of them provided technical corrections and proposed language changes, which we incorporated as appropriate. CDC and USAID suggested that we expand upon the discussion of the roles that they play in the global framework. USAID also recommended that we provide more information on difficulties commonly encountered in trying to carry out effective surveillance operations in developing countries. We inserted some additional information on relevant activities of CDC and USAID, as well as the problems often encountered in conducting infectious disease surveillance in developing countries.

SCOPE AND METHODOLOGY

To assemble the information required to produce this letter, we consulted with senior officials from WHO's Geneva and regional offices, CDC, the Departments of State and

²⁶This is one unit of the Division of Communicable Diseases.

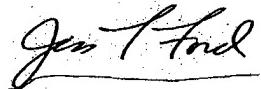
Defense, USAID, the multilateral development banks (the World Bank, the Inter-American Development Bank, the Asian Development Bank, and the African Development Bank), public health institutions in the state of Maryland, private foundations, and nongovernmental organizations. We examined documents generated by all of these institutions, including case histories of specific disease outbreaks. We obtained funding information from the U.S. agencies just cited, WHO, and the multilateral development banks.

We conducted our work from January through June 2000 in accordance with generally accepted government auditing standards.

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As agreed with your offices, unless you publicly announce the contents earlier, we plan no further distribution of this report until 2 days after its issue date. At that time, we will send copies of this report to interested congressional Committees; the Honorable Madeleine K. Albright, Secretary of State; the Honorable Donna Shalala, Secretary of Health and Human Services; the Honorable Lawrence H. Summers, the Secretary of the Treasury; the Honorable J. Brady Anderson, Administrator of USAID; the Honorable William Cohen, the Secretary of Defense; Dr. Gro Harlem Brundtland, Director General of the World Health Organization; and other interested parties. We will also make copies available to others on request.

Please contact me on (202) 512-4128 if you or your staff have any questions concerning this report. Key contributors to preparing this report were Lynne Holloway, Michael McAtee, Ann Baker, Kay Halpern, and Ashley Bander.



Jess T. Ford, Associate Director
International Relations and Trade Issues

DISEASE INFORMATION

This enclosure provides descriptive information on the diseases mentioned in the body of the letter. This information is derived primarily from WHO documents and was reviewed for accuracy by officials from CDC.

African trypanosomiasis, also known as sleeping sickness, is transmitted through the bite of the tsetse fly and can last for a few weeks to a several years. Early signs include fever, general weakness, headaches, and an aching sensation. Later symptoms include sleep disturbance, confusion, or convulsions, leading to permanent lethargy, coma, and death if left untreated. It is estimated that 300,000 people in 36 sub-Saharan African countries suffer from this disease. Available treatments are costly and dangerous, and some are losing their effectiveness. In addition, some drugs are no longer available.

Anthrax, a bacterial disease of animals, can be transmitted to humans in three ways, with varying results. Entry through the skin causes localized infection, and, if untreated, leads to death in 20 percent of cases. Inhalation generally leads to shock and death 1 to 2 days after the onset of acute symptoms. Anthrax occurs after the consumption of contaminated meat and causes inflammation of the intestinal tract, nausea, vomiting of blood, and severe diarrhea, with death occurring in 25-60 percent of cases. Anthrax can be treated with antibiotics and can be prevented through vaccination. The disease is present in agricultural regions worldwide.

Brucellosis, a disease of animals, is transmitted to humans through contact with infected animals or contaminated milk. Infection produces a wide range of symptoms, including fever, generalized aches and pains, and fatigue, which may last from a few weeks to several months. Brucellosis responds to the same antibiotics used to treat tuberculosis and is beginning to exhibit a similar drug resistance. The disease occurs worldwide.

Cholera is caused by a water- and food-borne bacterium. Infection results in acute watery diarrhea, leading to extreme dehydration and death if left unaddressed. Known vaccines and antibiotics have only limited impact on the disease – treatment focuses on rehydration. According to CDC, recent cholera outbreaks have killed about 1 percent of those becoming ill. A major international public health problem, cholera is prevalent in over 80 countries and causes over 100,000 deaths each year.

New-variant Creutzfeldt-Jakob disease was first described in March of 1996. The disease is believed to be transferred through consuming products from cows infected with bovine spongiform encephalopathy (mad cow disease). As of December 1999, there have been 50 reported cases, primarily in Great Britain. The disease starts out with depression or, less often, a schizophrenia-like psychosis. As the disease progresses, unsteadiness and involuntary movement occur, and shortly before death an infected person is rendered immobile and mute.

Crimean-Congo hemorrhagic fever is transmitted through tick bites or contact with bodily fluids of infected animals or people. It was first identified in 1944 in the Crimea

and has been found in Africa, Asia, the Middle East, and Eastern Europe. Symptoms are many and varied but can include hemorrhage, fever, dizziness, stiffness and muscle pain, nausea, mood swings, and sore eyes. This disease has a fatality rate of 30 percent. Blood transfusions and the drug ribavirin have been beneficial in treating the disease. A vaccine has been developed and used on a small scale but is not considered safe and effective for wider use.

Cryptosporidiosis is caused by a microscopic parasite. It can be spread through contaminated water, uncooked contaminated foods including fruits and vegetables, and any surface that has been in contact with the parasite. The parasite can survive outside the body for long periods of time and resists chlorine disinfection. Symptoms include diarrhea, stomach cramps or upset stomach, and a slight fever. People with weak immune systems may have more serious reactions. There is no effective treatment.

Dengue fever, a mosquito-borne infection caused by four distinct but closely related viruses, is a severe, flu-like illness with specific symptoms that vary based on the age of the victim. Dengue hemorrhagic fever is a potentially lethal complication that may include convulsions. There is no treatment for dengue fever beyond supportive therapy. With treatment, fatality rates can be less than 1 percent; without it, they can exceed 20 percent. There is no vaccine. Dengue is endemic in more than 100 countries and generates an estimated 50 million cases every year.

Diphtheria is a respiratory disease occurring worldwide that is spread through human-to-human contact. Symptoms range from mild to severe and can be complicated by damage to the heart muscle or peripheral nerves. The disease is fatal 5-10 percent of the time, even with treatment by administration of antibiotics and diphtheria antitoxin. Untreated, the fatality rate can be much higher. There is an effective vaccine for diphtheria, which is typically provided through national childhood vaccination programs.

Escherichia coli O157:H7 is a harmful strain of a bacteria commonly found in the gut of warm-blooded animals. It appears mainly in cattle and can be spread to humans through improperly prepared beef or milk products, as well as through other foods or the water supply. Symptoms can include abdominal cramps and watery or bloody diarrhea, usually without fever. Treatment with antibiotics is not recommended and may lead to more serious complications. According to CDC, about 3 to 5 percent of patients develop serious complications that can lead to kidney failure.

Ebola hemorrhagic fever, a viral disease, is transmitted by human-to-human contact, causing acute fever, diarrhea that can be bloody, vomiting, and a variety of other symptoms. There is no known cure, though some measures, including rehydration, can improve the odds of survival. Ebola kills more than half of those it infects. The Ebola virus was identified for the first time in 1976 and is still considered rare but has caused a number of outbreaks in central Africa.

Echinococcosis, also called Alveolar Hydatid disease, is caused by a parasitic tapeworm found worldwide but mostly in the Northern Hemisphere. Humans become infected by swallowing the tapeworm eggs, either on contaminated food, or after contact with an

animal carrier. Symptoms are slow to appear and usually involve the liver. They mimic liver cancer or cirrhosis and can include abdominal pain, weakness, and weight loss. Surgery is the most common form of treatment, although follow-up medication is often needed.

Encephalitis -- inflammation of the brain -- can be caused by a variety of infectious organisms.

Enterovirus 71 is one of several causes of hand-foot-mouth disease. This is a moderately contagious disease that is transmitted through human-to-human contact. Symptoms include fever, poor appetite, sores in the mouth, and a rash with blisters. It can lead to encephalitis. It occurs mainly in young children, but adults may also be at risk. The disease occurs worldwide, and there is no specific treatment for it beyond relief of specific symptoms.

Guinea worm disease, formally known as dracunculiasis, is transmitted in water contaminated with parasite larvae. The mature parasite conducts a painful journey through the body, usually emerging through the foot with intensely painful swelling and blistering. Perforation of the skin is accompanied by fever, nausea, and vomiting, and an infected person can stay ill for several months. Fatalities are rare, but secondary infection and permanent deformity can occur. According to CDC, the disease is present in 13 African countries.

HIV/AIDS: Human Immunodeficiency Virus is a disease of the immune system that leads to AIDS -- Acquired Immunodeficiency Syndrome. Weakened immune systems mean a greater susceptibility to opportunistic diseases like pneumonia and tuberculosis. The disease is transmitted through contact with bodily fluids of infected persons. Drugs are available that can prevent transmission from pregnant mothers to their unborn children. These same drugs can help slow the disease. As of December 1999, 33.6 million people worldwide were living with HIV/AIDS.

Hendra virus causes disease in both humans and many species of animals. In humans, it causes a respiratory disease that is often fatal. It was discovered in 1994, and is not found outside of Australia.

Human monkeypox is caused by a virus related to smallpox and is susceptible to the smallpox vaccine. Since the smallpox vaccine is no longer used, monkeypox is becoming an increasing concern in Central and Western Africa. It is transmitted to humans through contact with infected animals and appears to be increasingly transmittable through human-to-human contact. Fatality rates have ranged between 2 and 10 percent.

Influenza, or flu, is a respiratory infection caused by three types of virus, of which two (Influenza types A and B) lend themselves to epidemics and are found worldwide. There is an influenza vaccine, but the viruses change so quickly that the vaccine must be updated every year. Several drugs exist to treat influenza.

Japanese encephalitis is a mosquito-borne viral disease. Infection can be mild, with only fever and headache, to severe, with neck stiffness, stupor, tremors, spastic paralysis, and coma. There are 30,000 to 50,000 cases annually, with a 30-percent fatality rate. The disease occurs primarily in Asia and is not treatable beyond supportive therapy. There is a vaccine available, but it is expensive and occasionally causes adverse reactions.

Lassa fever is caused by a virus transmitted through contact with infected rats. It occurs in Africa and was first described in the 1950s. Symptoms include deafness, fever, nausea, vomiting, diarrhea, and, in more severe cases, seizures and hemorrhage. This disease has a fatality rate of 15 percent and is difficult to distinguish from several other diseases. No vaccine is currently available, although ribavirin has been used as a preventative measure as well as to treat the disease.

Leishmaniasis, a parasitic disease transmitted by sandflies, is endemic in 88 countries, affecting an estimated 12 million people. There are four types. Visceral leishmaniasis is the most severe form, causing irregular bouts of fever, weight loss, swelling of the spleen and liver, and anemia. If untreated, it has a fatality rate of almost 100 percent. Mucocutaneous leishmaniasis produces disfiguring lesions on the mucous membranes. Cutaneous leishmaniasis produces ulcers on exposed parts of the body and can lead to permanent scarring or disfigurement. Diffuse cutaneous leishmaniasis never heals on its own and often relapses. Leishmania/HIV co-infections occur frequently.

Leptospirosis is a bacterial disease transmitted via the urine of infected animals contaminating water, food, or soil. It occurs worldwide but is most common in temperate or tropical climates. According to CDC, this disease is particularly difficult to diagnose. Symptoms can include fever, chills, muscle aches, vomiting, diarrhea, hemorrhage, and respiratory failure. Some cases progress to a second phase, which can include kidney or liver failure or meningitis. In rare cases, death occurs. Leptospirosis is treatable with antibiotics, especially when given early in the course of the disease.

Lyme borelliosis, or Lyme disease, is a bacterial illness transmitted by ticks. The area around the tick bite develops a "bull's eye" rash, typically accompanied by fever, headache, and musculoskeletal aches and pains. If untreated by antibiotics, arthritis, neurologic abnormalities, and, rarely, cardiac problems follow. It is rarely, if ever, fatal. There is an effective vaccine for adults at high risk.

Malaria is a tropical parasitic disease, transmitted by mosquitoes and endemic in 101 countries and territories. About 40 percent of the world population is considered at risk for malaria. Ninety percent of the cases are in sub-Saharan Africa, but malaria is now reemerging in countries where it was once under control. Symptoms include fever, shivering, pain in the joints, headache, repeated vomiting, convulsions, coma, and in severe cases, death. Malaria is becoming increasingly resistant to known primary drug treatments.

Measles is a highly contagious viral disease that often strikes children, causing fever, conjunctivitis, congestion, and cough, followed by a rash that lasts 2 to 4 days. This

disease is transmitted through human-to-human contact, and secondary infections often cause further complications. Sustained efforts to immunize children have reduced the prevalence of this disease, but it still occurs worldwide, with an estimated 31 million cases leading to 1 million deaths every year.

Meningitis, a condition that may be caused by several disease agents, is an infection and severe inflammation of the fluid membranes that surround the brain and spinal cord. Meningococcal meningitis, caused by a particular type of bacteria, is characterized by sudden onset of fever, headache, neck stiffness, and altered consciousness and is transmitted by person-to-person contact. Untreated epidemics can incur fatality rates of over 50 percent. However, epidemic fatality rates in the last 30 years have generally been in the 8-12 percent range. There is a vaccine for this disease, but it loses its effectiveness over time and must be repeated.

Nipah virus is a newly emerging disease causing encephalitis. It is believed to be transmitted through contact with infected pigs. Symptoms include headache, fever, muscle spasms, coma, and brain damage. There is no treatment beyond alleviation of symptoms.

Omsk hemorrhagic fever is caused by a virus in the same family as the viruses causing yellow fever, Japanese encephalitis, West Nile fever, and dengue. It is found only in central Russia.

O'nyong-nyong fever is a viral illness spread by mosquitoes. It causes symptoms such as joint pain, rash, high fever, and eye pain. Fatalities are rare. Epidemics of this virus have occurred twice since its appearance in 1962 in Africa.

Pertussis, or whooping cough, is a highly contagious bacterial disease found worldwide, mostly in developing countries. There are 20 million to 40 million cases with 200,000 to 300,000 deaths every year. It is spread through human-to-human contact, in the air. Symptoms include runny nose and sneezing, a mild fever, and a cough that gradually becomes more severe, turning into paroxysms of coughing that cause vomiting and exhaustion. Pertussis is treatable with antibiotics. Pertussis vaccine is commonly administered as part of routine childhood immunization programs.

Plague is a severe bacterial infection that is usually transmitted to persons by infected rodent fleas (bubonic plague) and uncommonly by person-to-person respiratory exposure (pneumonic plague). Symptoms of bubonic plague include swollen, painful lymph glands ("buboies"), fever, chills, headache, and exhaustion. Persons with pneumonic plague develop cough, bloody sputum, and breathing difficulty. Plague is treatable with antibiotics. However, unless diagnosed and treated early, it is highly fatal. There are an estimated 1,000 to 3,000 cases of plague worldwide each year.

Poliomyelitis, or polio, is a virus transmitted through human-to-human contact. In most cases, there are no symptoms, or only mild, flu-like symptoms. Five to 10 percent of the cases can lead to aseptic meningitis, while only 1 percent of infections lead to the acute flaccid paralysis typically associated with polio. There is an effective vaccine,

commonly included as part of routine childhood vaccination. However, the disease is still considered endemic in 61 countries.

Rabies is a viral disease transmitted through contact with the saliva of infected animals. It is estimated that 40,000 to 70,000 people die from it every year. Symptoms progress from respiratory, gastrointestinal, or central nervous system affliction to hyperactivity to complete paralysis, coma, and death. Once symptoms start to appear, the disease is not treatable. Multiple-dose courses of vaccine and immunoglobulin can be used to prevent onset of the disease if administered immediately after contact with a suspected carrier.

Reston virus is a variety of the Ebola virus found in Asia. It is found mostly in monkeys. Humans can become infected with Reston virus and produce antibodies but do not suffer from the effects of a hemorrhagic fever.

Rift Valley fever is caused by a virus transmitted by mosquitoes or contact with body fluids of infected animals or people. The disease was first detected at the turn of the century and occurs in many parts of Africa. Rift Valley fever usually causes a flu-like illness lasting 4 to 7 days, but about 1 percent of the cases develop into a more severe hemorrhagic fever, with an approximately 50 percent fatality rate. No treatment for Rift Valley fever has been found, beyond supportive measures. Vaccines are being developed, but they are not yet widely available for human use.

River blindness, or onchocerciasis, is a parasitic disease endemic in 37 countries, nearly all in Africa. Blackflies transmit the larva to humans, where it grows into a parasitic worm with a lifespan of 12 to 15 years. This worm spawns millions of microscopic parasites, which travel throughout the body, causing unbearable itching, skin disfigurement, and vision impairment or blindness. Treatment with the drug ivermectin kills the infant parasites but has very limited effect on the adult worms, if any.

Ross River virus is a mosquito-borne disease found in Australia that cannot be treated beyond relief of symptoms. Symptoms include swollen joints, sore muscles, rash, fever, sore throat, and fatigue.

Tetanus, or lockjaw, is caused by a toxin produced by a bacterium found in the intestines of many animals and in the soil. It is transmitted to humans through open wounds, and is a particular problem in newborn infants because of unsanitary birthing practices. Symptoms include generalized rigidity and convulsive spasms of skeletal muscles. It is fatal about 30 percent of the time. It can be treated with an antitoxin, and there is an effective vaccine, commonly included in childhood vaccination programs. Tetanus occurs worldwide.

Tuberculosis is an airborne contagious disease that is estimated to kill 2 million people each year. Over one-third of the world's population is thought to be infected. A person with a healthy immune system can become infected, but not fall ill. Symptoms of tuberculosis can include a bad cough, coughing up blood, pain in the chest, fatigue, weight loss, fever and chills. There are several drugs that can be used to treat

tuberculosis, but the disease is becoming increasingly drug resistant. The available vaccine, commonly administered to children, has only a limited effect.

Typhoid fever is a bacterial illness that occurs worldwide, mostly in developing countries. It is spread through contaminated food and water and causes a high fever, stomach pains, and sometimes a rash. It is treatable by antibiotics, and there is a vaccine, although it is not 100 percent effective. If untreated, the disease causes death in 20 percent of cases.

Venezuelan equine encephalitis is a mosquito-borne viral disease that can be transmitted to humans from equine hosts. Symptoms in humans include flu-like symptoms of fever and headache. Severe illness and death can occur in the young and the elderly and those with weakened immune systems.

West Nile fever is a mosquito-borne viral encephalitis. Symptoms include fever, head and body aches, rash, and, in more serious cases, stupor, coma, convulsions, and paralysis. Death occurs in 3-15 percent of cases. There is no vaccine for the West Nile virus, and it is not treatable beyond supportive therapies. It occurs in Africa, Eastern Europe, West Asia, the Middle East, and, most recently, in the United States.

Yellow fever is a mosquito-borne virus, endemic in over 40 countries of Africa and Central and South America and constituting an estimated 200,000 cases and 30,000 deaths every year. Symptoms include fever, muscle pain, headache, loss of appetite, and nausea. Fifteen percent of patients progress to a toxic phase, which can include jaundice, abdominal pain, and bleeding from the mouth, nose, eyes, or stomach. The kidneys deteriorate and may fail. Half of the patients who enter this phase die. There is no treatment for yellow fever beyond supportive therapies. A safe and highly effective vaccine for yellow fever is available but is often not included in national vaccination programs.

OUTBREAK RESPONSE – RIFT VALLEY FEVER 1998

Beginning in October 1997, unusually heavy rains swept across Kenya and adjacent parts of Somalia. As the rains continued, flooding began to occur. By December 1997, local officials in Kenya began to receive reports of unusually high levels of fatal hemorrhagic illness among domestic animals. These reports were soon followed by reports of acute fever in humans, accompanied by severe headache, muscle pain, hemorrhage, vomiting, and diarrhea. In late December, the Kenyan Ministry of Health and the World Health Organization (WHO) office in Nairobi were informed that nearly 500 people had died from this unexplained illness – some of them within 24 hours of becoming ill. Concerned institutions, including the Ministry, the WHO missions in Kenya and Somalia (where cases had also been detected), Doctors Without Borders, the African Medical and Research Foundation, and the Kenyan Medical Research Institute, established a task force to look into this outbreak.

Shortly thereafter, officials from WHO, the International Federation of the Red Cross, the African Medical and Research Foundation, the Kenyan Ministry of Health, Doctors Without Borders, and Médecins du Monde participated in a field investigation. By December 30, analysis of tissue samples by South Africa's National Institute for Virology and CDC showed that a substantial portion of the deaths being reported were caused by Rift Valley fever, while others were caused by other hemorrhagic fever pathogens.

When the disease diagnosis had been confirmed, the task force devised and launched a public education campaign on how to deal with the outbreak. (For example, people in affected areas were advised not to slaughter sick animals.) Health care workers were informed about appropriate case management techniques. Large-scale active surveillance and response efforts were organized, with helicopter transport provided by the Kenyan government, WHO, and international relief organizations.

The task force established four research groups to investigate the outbreak's human epidemiology, to conduct laboratory investigations, and to study veterinary and entomological aspects of the event. Two teams from CDC assisted in defining the prevalence of Rift Valley Fever infection and the geographic distribution of the outbreak in Kenya and neighboring countries. Four U.S. Department of Defense laboratories, including the U.S. Army Medical Research Unit in Kenya, also made contributions to these epidemiological investigations. The U.S. Naval Medical Research Unit in Egypt established a capability to perform Rift Valley fever diagnostic assays, and the U.S. Army Research Institute of Infectious Diseases in Maryland supplied human Rift Valley Fever vaccine (not yet approved for general use) to immunize at-risk laboratory workers.

International efforts to investigate and provide an effective response to this outbreak were complicated by transportation difficulties (flooding, poor roads), lack of security in regions along the Kenya-Somalia border, and the fact that nurses and lab personnel in Kenya were on strike during the outbreak. Ultimately, though precise estimates are impossible, health officials estimate that at least 89,000 persons became ill during the outbreak – though in many the illness was limited to its milder (nonfatal) form. At the same time, livestock owners reported losing substantial portions of their herds.

WHO COLLABORATING CENTERS FOR ARBOVIRUSES AND
HEMORRHAGIC FEVERS

Instituto Nacional de Enfermedades Virales, Pergamino, Argentina
Queensland University of Technology, Brisbane, Australia
University of Western Australia, Nedlands, Australia
Instituto Adolfo Lutz, Sao Paulo, Brazil
Instituto Evandro Chagas, Belem, Brazil
Laboratory Centre for Disease Control, Ottawa, Canada
Institut Pasteur de Bangui, Central African Republic
Instituto de Medicina Tropical Pedro Kouri, Havana, Cuba
University of Helsinki, Finland
Institut Pasteur, Paris, France
Aristotelian University of Thessaloniki, Greece
National Institute of Virology, Pune, India
U.S. Naval Medical Research Unit No. 2, Jakarta, Indonesia
Instituto Superiore di Sanità, Rome, Italy
Nagasaki University, Japan
Kenya Medical Research Institute, Nairobi, Kenya
Asan Institute for Life Sciences, Seoul, Republic of Korea
University of Malaya, Kuala Lumpur, Malaysia
Erasmus University Hospital, Rotterdam, Netherlands
University of Ibadan, Nigeria
Ivanovsky Institute of Virology, Moscow, Russia
Chumakov Institute of Poliomyelitis and Viral Encephalitides, Moscow, Russia
Institut Pasteur de Dakar, Senegal
Slovak Academy of Sciences, Bratislava, Slovak Republic
Institute of Microbiology and Immunology, Ljubljana, Slovenia
National Institute for Virology, Sandringham, South Africa
Swedish Institute for Infectious Disease Control, Stockholm, Sweden
Uganda Virus Research Institute, Entebbe, Uganda
Public Health Laboratory Service, London, United Kingdom
Centers for Disease Control and Prevention, Atlanta, Georgia
Centers for Disease Control and Prevention, Fort Collins, Colorado
Centers for Disease Control and Prevention, San Juan, Puerto Rico
University of Texas Medical Branch, Galveston, Texas
U.S. Army Medical Institute of Infectious Diseases, Fort Detrick, Maryland

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